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EXAMINER

SANDALS, WILLIAM O

ART UNIT PAPER NUMBER

1636

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21

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.  
09/544,045

Applicant(s)  
Sauer et al.

Examiner  
William Sandals

Art Unit  
1636



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Dec 27, 2002
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-49 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-49 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some\* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_ 6) ☐ Other:

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## DETAILED ACTION

### *Status of the Claims*

1. Claims 1-49 are pending. Claims 50-65 have been cancelled by amendment in Paper No. 19, filed December 27, 2002.
2. The rejection of claims 1-6 and under 35 USC 102 over Serre et al. in the previous office action has been withdrawn.
3. Claims 1-47 and 49 stand rejected under 35 USC 112, first paragraph. The response to the arguments is contained in the rejection repeated below.
4. Claims 1-6 and 21 stand rejected under 35 USC 102(b) over Miller et al. The response to the arguments is contained in the rejection repeated below.
5. Claims 1-6 and 21 stand rejected under 35 USC 102(b) over Ackroyd et al. The response to the arguments is contained in the rejection repeated below.
6. Claims 1-30, 32-45 and 47-49 stand rejected under 35 U.S.C. 103(a) as being obvious over each of Miller et al. or Ackroyd et al. in view of US 5,677,177 (Wahl et al.). The response to the arguments is contained in the rejection repeated below.

### *Response to Arguments*

7. The sustained rejections and responses to arguments in Paper No. 19 follow:

#### *Claim Rejections - 35 USC § 112*

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-47 and 49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the practice of the method *in vitro* and in cells in culture, does not reasonably provide enablement for practice of the method in a multicellular organism or animal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to a method of identifying variant recombinases that mediate recombination at variant recombination sites. While applicants have shown the practice of the method *in vitro* and in cells in culture, they have not demonstrated any practice of the method in a multicellular organism or animal. In order to do so, undue experimentation is required. Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors. Many of these factors have been summarized in *In re Wands*, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988).

The Wands factors as they apply to the instant claimed invention are as follows:

- a- The quantity of experimentation necessary to reduce the instant claimed invention to practice would involve demonstration of the ability to practice the method in a multicellular organism or animal.

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b- The only working examples presented in the instant specification are done *in vitro*, and no examples of practice of the invention are presented method in a multicellular organism or animal.

c- The nature of the invention is complex. Gene therapy is a new and developing art as recited in Marshall in the section titled "The trouble with vectors", and at page 1054, column 3, and at page 1055, column 3. The problems of gene delivery, gene targeting to reach the intended host cell, and then to reach the intracellular target are not yet solved, as taught in Verma et al. (see especially page 239, column 3, the box titled "What makes an ideal vector?" and page 242).

d- The prior art taught by Orkin et al. (see especially the section on "Gene transfer and expression" and "Gene therapy in man status of the field") described many problems in the developing field of gene therapy. Recited problems include: lack of efficacy, adverse short term effects and limited clinical experience, the inability to extrapolate experimental results and unreliability of animal models. Problems with the vector include: host immune response to the vector and the expressed product, difficulty of targeting the vector to the desired site, transient expression of the gene of interest and low efficiency of delivery of the vector to the targeted site.

f- The relative skill of those in the art as taught by Verma et al., which states "the problems - such as the lack of efficient delivery systems, lack of sustained expression, and host immune reactions - remain formidable problems" and Anderson, W. F. (see page 25, top of column 1), which states "[e]xcept for anecdotal reports of individual patients being helped, there is still no conclusive evidence that a gene-therapy protocol has been successful in the treatment of human disease".

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g- The art is unpredictable, since a negative result which may result from any one of the above mentioned "problems" cannot be explained by the teachings of those of skill in the art. The instant claims and specification must therefore provide the necessary teachings to enable the use of the instant claimed method in a multicellular organism or animal. Such teachings are not found in the instant claims or specification.

h- Therefore, given the analysis above, it must be considered that the skilled artisan would have needed to have practiced considerable non-routine, trial and error experimentation to enable the full scope of the claims.

#### ***Response to Arguments***

10. Regarding the standing rejection of claims 1-47 and 49 under 35 USC 112, first paragraph, Applicants have argued in Paper No. 19, at page 2, that "[i]f the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate".

The prior art as recited in Sigmund at the abstract states "[b]ecause the use of transgenic and gene-targeted models has increased in popularity, the number of reports describing unpredictable phenotypic effects caused by variation in the genetic background used to generate or propagate these animals has steadily increased. There are now many examples in which animals containing the same exact genetic manipulation exhibit profoundly different phenotypes when present on diverse genetic backgrounds, demonstrating that genes unrelated, per se, to the ones being targeted can play a significant role in the observed phenotype." Jaroff quotes

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Anderson at pages 69, column 2, "except for reports of individual patients being helped, 'there is still no conclusive evidence that a gene-therapy protocol has been successful in the treatment of human disease". Wall recites at page 58, first paragraph, "[a] Medline search reveals that over 6000 scientific articles have been published in which transgenic animals (mostly mice) were used to answer basic research questions. By contrast, 289 papers dealt mostly with transgenic livestock of which 24% were reviews. The limited publication record for transgenic livestock species reflects the high costs and technical difficulties associated with producing transgenic livestock more than lack of applicability of this technology to farm animals." Each of these reports emphasize the lack of understanding and lack of predictability of animal models. Animal models are not recognized as "correlating" as stated in the rejection above. The practice of gene expression in animals is unpredictable because of the "lack of efficacy, adverse short term effects and limited clinical experience, the inability to extrapolate experimental results and unreliability of animal models". The teachings of these references make it abundantly clear to one of skill in the art that there is a fundamental lack of information on how to effect gene transfer and how to reliably predict gene activity in animal models. The argument is therefore, not found convincing.

11. Applicants have argued in Paper No. 19, page 2, that the method is simple and able to function in yeast and mammalian cells.

The rejection of scope of enablement above is directed to the practice of the invention in a multicellular organism or animal. An amendment to the claims stating that the practice of the

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invention is limited to "*in vitro* and cells in culture", cancelling or amending claims 43, 44 and 46 as required, would be found sufficient to overcome the rejection. The argument is moot in view of the above rejection.

12. Applicants have argued in Paper No. 19, pages 2-3 that methods of using Cre recombinase *in vivo* have been extensively studied, thereby making the practice of the claimed invention enabled.

This statement does not present any facts to support the assertion or argue why the statement should be found convincing. The method as taught in the instant claims and specification (especially at pages 95-97), describe the practice of the invention in cells in culture, and do not extend any teachings to the practice of the invention in a multicellular animal. A fair reading of the teachings of the instant specification supports the definition of the phrase "*in vivo*" to mean "in cells in culture". A broad interpretation of the meaning of the phrase "*in vivo*" to mean practicing the instant invention in a multicellular organism or animal, is not supported by the specification. Thus, the argument is not found convincing.

13. Applicants have argued in Paper No. 19, page 3, lines 4-11 that the claims are drawn to a method of identifying variant recombinases.

Claims 1-23 are drawn to a method of identifying variant recombinases. Dependent claims 24-49 are drawn to a method of producing site specific recombination, and claims 43, 44 and 46 are specifically drawn to practice of the invention in a multicellular organism, which may be a mammal. Independent claims must embrace all of the limitations of the dependent claims,



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thereby making all of claims 1-49 readable on the practice of the invention in a multicellular organism or animal. This being the case, the rejection above is appropriate, and the rejection is sustained. An amendment to the claims stating that the practice of the invention is limited to "*in vitro* and cells in culture", cancelling or amending claims 43, 44 and 46 as required, would be found sufficient to overcome the rejection.

***Claim Rejections - 35 USC § 102***

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 1-6 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Miller et al.

Miller et al. teach (see especially the introduction, figures and materials and methods):

- A) a method bringing into contact a mutant *Int* recombinase
- B) with a pair of mutant *Att* recombination sites or a pair of wild type recombination sites, which are comprised on first and second nucleic acid sequences (constructs)
- C) comparing the activity of the mutant recombinase on the mutant recombination sites to the activity of the wild type recombinase on the mutant recombination sites (see Miller et al. at the introduction and page 725, column 2 "Discussion")

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D) the mutant recombination sites may have identical sequences (see Miller et al. at page 723, column 2)

E) the mutant recombination sites may not recombine with the wild type recombination sites (see Miller et al. at the introduction)

E) the mutant recombination sites may have significant reduction in recombination frequency with wild type recombinase

F) the constructs with the recombination sites alter the expression of the reporter gene when the recombination sites are recombined.(see Miller et al. at page 725, column 2 "Discussion")

***Response to Arguments regarding Miller et al.***

16. In response to the rejection in the previous office action of claims 1-6 and 21 under 35 USC 102(b), Applicants have argued in Paper No. 19, page 4, lines 4 bridging to page 5, line 2, that Miller et al. teaches recombination sites which are not recombinant, but are wild type *int* recombination sites, or where recombination occurs between a variant recombination site and a wild type recombination site.

Miller et al. teach at page 725, column 2 bottom, (Discussion), bridging to page 726, column 1, top, "[i]n this study we report the isolation of a mutation, *int*-h3, that results in the expression of a lambda integrase exhibiting enhanced activity. This activity is manifested by the ability to support lambda site-specific recombination under two conditions where wild-type integrase exhibits low activity: in bacterial mutants that fail to support lambda site-specific

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recombination, and under conditions where the recombinational *att* sites are altered.” This conforms to the requirement of instant claim 1, lines 16-18 which recites “wherein recombination between the third and fourth recombination sites indicates that the mutant recombinase retains the ability to mediate recombination at non-variant recombination sites”. The cited section of Miller et al. above, states that the mutant integrase recombines sequences with altered recombination sites. Therefore, the argument is not found convincing.

17. Claims 1-6 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Ackroyd et al.

Ackroyd et al. teach (see especially the abstract, introduction, Table 1, the figures and pages 637-638):

- A) a method bringing into contact a mutant recombinase
- B) with a pair of mutant recombination sites or a pair of wild type recombination sites, which are comprised on first and second nucleic acid sequences (constructs) (see Table 1)
- C) comparing the activity of the mutant recombinase on the mutant recombination sites to the activity of the wild type recombinase on the mutant recombination sites (see page 637, column 2, and Table 1)
- D) the mutant recombination sites may have identical sequences (see Table 1)
- E) the mutant recombination sites may not recombine with the wild type recombination sites (see Table 1)

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E) the mutant recombination sites may have significant reduction in recombination frequency with wild type recombinase

F) the constructs with the recombination sites alter the expression of the reporter gene when the recombination sites are recombined (see Table 1).

***Response to Arguments regarding Ackroyd et al.***

18. In response to the rejection in the previous office action of claims 1-6 and 21 under 35 USC 102(b), Applicants have argued in Paper No. 19, page 5, line 11 bridging to page 6, line 5 that Ackroyd et al. teach two wild-type resolvases Tn3 and Tn21, and teach mutants which have activities like their wild-type counterparts.

Ackroyd et al. teach at the abstract, that the Tn3 resolvase was mutated by changing an amino acid to a corresponding amino acid from Tn21. By changing the amino acids in a methodical and processive method, the mutated Tn3 resolvases are tested for activity on wild-type Tn3 and Tn21 recombination sites. Mutated Tn3 resolvases retain their ability to recombine at the wild-type Tn3 and are now able to recombine at wild-type Tn21 recombination sites. The Tn21 recombination sites of Ackroyd et al. correspond to the instant claimed variant recombination sites with respect to the instant claimed mutated Tn3 resolvases. This satisfies the limitations of the claims. The argument is therefore, not found convincing.

19. In response to the rejection in the previous office action of claims 1-6 and 21 under 35 USC 102(b), Applicants have argued in Paper No. 19, page 6, lines 1-5 that in the instant claimed invention, variant recombination sites are not recognized by non-mutant recombinases.

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Instant claim 3 recites that the recombination frequency between the first and second recombination sites (which are the variant recombination sites) is significantly reduced. This being the case, in the instant claimed invention, it is permissible for the non-mutant recombinase to recognize the variant recombination sites. The argument is therefore, not found convincing.

***Claim Rejections - 35 USC § 103***

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

21. Claims 1-30, 32-45 and 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of Miller et al. or Ackroyd et al. in view of US 5,677,177 (Wahl et al., of record).

The claims are drawn to a method to identify a mutant recombinase, where the mutant recombinase is tested for activity on wild type and mutant recombination sites as recited in claims 1-23. Dependent claims 24-49 are drawn to a method of producing site-specific recombination. The mutant recombination sites (first and second sites) are on a first nucleic acid and the wild type recombination sites (third and fourth) are on a second nucleic acid. The wild type and mutant recombination sites are linked to reporter genes. The mutant recombinase has greater activity with the mutant recombination sites than with the wild type recombination sites, and the wild type recombinase has lowered activity with the mutant recombination sites. The

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mutant recombination sites may be identical, and the wild type recombination sites may be identical as recited in claim 4. The first and second nucleic acids contain a structural gene, an enzyme or a regulatory molecule as recited in claims 28, 32 and 45. The recombination of the first and second recombination sites alters expression of the first reporter and recombination between the third and fourth recombination sites alters expression of the second reporter as recited in claims 5-23. The reporter gene expression may be activated or inactivated by the removal of a spacer in, or near the reporter which blocks expression of the reporter gene. The reporter gene may be excised from the construct as recited in claims 7, 10, 13-16, 19 and 45-47. The reporter gene may be activated or inactivated by an inversion of part or all of the reporter gene as recited in claims 8, 11, 17, 20 and 33-45. The first and second nucleic acid sequences may be connected by a preselected DNA segment as recited in claims 26-35 and 45-47. The mutant recombinase may be further tested for activity on one or more additional recombination sites as recited in claims 24-49. The recombination reaction may occur *in vitro* or may occur in a cell which may be in a prokaryotic cell or a eukaryote cell. The eukaryotic cell may be in multicellular organism, a plant or a mammal as recited in claims 43, 44 and 46.

Miller et al. teach (see especially the introduction, figures and materials and methods) a method bringing into contact a mutant *Int* recombinase with a pair of mutant *Att* recombination sites or a pair of wild type recombination sites, which are comprised on first and second nucleic acid sequences (constructs), comparing the activity of the mutant recombinase on the mutant recombination sites to the activity of the wild type recombinase on the mutant recombination

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sites. The mutant recombination sites may have identical sequences. The mutant recombination sites may not recombine with the wild type recombination sites. The mutant recombination sites may have significant reduction in recombination frequency with wild type recombinase. The constructs with the recombination sites alter the expression of the reporter gene when the recombination sites are recombined.

Ackroyd et al. teach (see especially the abstract, introduction, Table 1, the figures and pages 637-638) a method bringing into contact a mutant recombinase with a pair of mutant recombination sites or a pair of wild type recombination sites, which are comprised on first and second nucleic acid sequences (constructs), comparing the activity of the mutant recombinase on the mutant recombination sites to the activity of the wild type recombinase on the mutant recombination sites. The mutant recombination sites may have identical sequences. The mutant recombination sites may not recombine with the wild type recombination sites. The mutant recombination sites may have significant reduction in recombination frequency with wild type recombinase. The constructs with the recombination sites alter the expression of the reporter gene when the recombination sites are recombined.

Each of Miller et al. or Ackroyd et al. did not teach that the first and second nucleic acids may be linked by a DNA segment, nor the deletion or excision of the reporters or spacers, nor inversion of the reporters to switch on or switch off expression of the reporters. Also not taught was the performance of the method in a eukaryotic cell.

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Wahl et al. teach (see especially the abstract, Brief Description, figures and columns 3-8) the well known use of a recombinase to insert, invert and delete a sequence in a construct. Wahl et al. teach the inactivation or activation of a desired gene sequence, such as a reporter, in a mammalian cell by the insertion, inversion or inactivation of a DNA segment using site-specific recombination (see especially columns 5-6).

One of ordinary skill in the art would have been motivated to modify the method of bringing into contact a mutant recombinase with either a pair of mutant recombination sites or a pair of wild type recombination sites, which are comprised on first and second nucleic acid sequences (constructs) to compare the activity of the mutant recombinase on the mutant recombination sites to the activity of the mutant recombinase on the wild-type recombination sites of each of Miller et al. or Ackroyd et al. with the practice of recombining DNA segments by site-specific recombination in mammalian cells of Wahl et al. to produce a method to use a mutant recombinase to insert, invert and delete sequences in a construct to inactivate or activate a desired gene sequence, for the expected benefit of being able to introduce a gene into a mammalian cell in one form and then be able to modify the introduced gene in a defined manner where the desired, recombined nucleic acid sequence may be useful as a reporter in a mammalian cell, or may be used to modify the phenotype of the mammalian cell (see Wahl et al. at column 2, lines 19-40). Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of



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Miller et al., Ackroyd et al. and Wahl et al. who demonstrate a method of site-specific recombination to deliver a desired gene into a cell.

***Response to Arguments Regarding the Obviousness Rejection***

22. In response to the rejection in the previous office action of claims 1-6 and 21 under 35 USC 103(a), Applicants have argued in Paper No. 19, page 6, line 61 bridging to page 7, line 4 that Wahl et al. do not make up for the deficiencies of either Miller et al. or Ackroyd et al. in teaching the identification of a mutant recombinase.

Since both Miller et al. and Ackroyd et al. teach the invention as described in the rejections under 35 USC 102(b) above, there being no deficiencies to make up for, the argument is not found convincing.

***Conclusion***

23. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

24. Certain papers related to this application are *welcomed* to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If

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applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.


Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Thursday from 8:30 AM to 7:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Tech Center customer service center at telephone number (703) 308-0198.

William Sandals, Ph.D.

Examiner

March 20, 2003

  
REMY YUCEL, PH.D  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600